NATIONAL INSTITUTES OF HEALTH

FISCAL YEAR 2004

PLAN FOR HIV-RELATED RESEARCH

XII: TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

OFFICE OF AIDS RESEARCH

AREA OF EMPHASIS:

Training, Infrastructure, and Capacity Building

SCIENTIFIC ISSUES

African American and Latino populations—both women and men—bear the large proportion of newly HIV-infected individuals in the United States. To curb this trend, it is essential to develop cultural- and ethnic-sensitive programs to encourage African and Hispanic Americans' participation in HIV prevention and research.

Programs tailored to minorities are needed to motivate young students, starting at the high school level, to consider careers in science in order to create a pool of professionals to be trained to perform HIV/AIDS-related research. Well-trained biomedical and behavioral minority HIV/AIDS investigators as well as individuals trained in technical support areas are urgently needed. To accomplish this need, new mechanisms for the HIV/AIDS research training should be in place to attract not only newly recruited and trained young scientists, but also established scientists from related fields. Mentoring opportunities are essential for the success of the training programs.

In-country training programs for biomedical and behavioral personnel are required to conduct therapeutic and prevention clinical trials in developing countries greatly affected by the HIV/AIDS epidemic. Expansion of these programs must include training in ethics issues (providing materials in the native language especially for the establishment of ethics boards), clinical trials, behavior sciences, technology transfer, and informatics.

In addition to well-trained personnel, a suited infrastructure must be in place to conduct HIV-related research both in the United States and in foreign research institutions. Both the United States and developing countries need to have sufficient infrastructure for supporting the research, including appropriately equipped laboratories, computer and data management capabilities, inpatient and outpatient space for clinical research, and associated health and laboratory personnel. Mechanisms for long-term infrastructure maintenance in developing countries need to be implemented.

HIV/AIDS biomedical prevention (e.g., vaccines and microbicides) and antiretroviral drugs testing depend mainly on the use of nonhuman primate (NHP) models. Expanded animal facilities are still needed, not only to house experimentally infected NHP (biosafety level [BSL] BSL-2/ -3 facilities) but also to breed the appropriate number of specific pathogen-free (SPF) animals required for HIV/AIDS research.

TRAINING PROGRAMS

Though NIH-funded programs have expanded the number of training positions in AIDS-related research, an increased focus on African American and Latino trainees is needed. The predoctoral and postdoctoral training supported by NIH from non-AIDS funds that provides broad interdisciplinary training and prepares investigators to undertake AIDS-related research must also be tailored to fulfill the needs of the highly affected minority population.

The NIH Loan Repayment Program (LRP) was mandated by Congress under Public Law 100-607 in 1988, authorized under 42 USC 288-1, and re-authorized under Public Law 103-43 to encourage health professionals to engage in AIDS-related research at NIH. Since the program enrolled the first participants in 1989, 134 professionals (through FY 2001) have been attracted to the NIH intramural research program to receive the benefits of NIH's loan repayment. More than half of participants have continued longer than their contractually obligated period. This program should be expanded to attract more qualified African American and Hispanic graduates to NIH.

The Fogarty International Center (FIC) has two programs, the AIDS International Training and Research Program (AITRP) and the Fogarty International Research Collaboration Award for AIDS (FIRCA), to support training in AIDS-related research in resource-poor countries. The AITRP is a multidisciplinary program designed to strengthen research capacity in the epidemiology, prevention, diagnosis, and treatment of HIV/AIDS in developing countries; to facilitate the evaluation of AIDS drugs and vaccines

internationally; and to provide global scientific leadership in HIV/AIDS. AITRP is active in 92 developing countries; its activities are focused in the countries that have the most serious current or emerging HIV/AIDS epidemics. FIRCA provides support for collaboration between U.S. and foreign scientists, in the foreign partner's laboratory, through a grant to a U.S. investigator who is already funded to conduct HIV-related research. The FIC research training programs have facilitated the conduct of many research studies supported by other NIH Institutes and Centers (ICs) in a wide range of research disciplines. However, more and better programs have to be in place to cease the AIDS epidemic in the world.

The National Cancer Institute (NCI) has addressed, domestically, the training need for clinicians and clinical researchers to study AIDS-related malignancies. This training should increase the number of participating minority institutions and investigators.

The National Institute of Mental Health (NIMH), through the Center for AIDS Prevention Studies (CAPS) in San Francisco, supports two model training programs: a minority investigators training program to provide mentoring and technical assistance to minority visiting professors who plan to conduct research on HIV risk behavior in minority populations; and an international scholars program, which provides research training for international scientists and builds partnerships to promote productive international research with these scholars. These programs may be duplicated by other ICs to stimulate not only prevention studies but also basic and clinical research projects.

In different parts of the world, the epidemic is driven by injecting drug users (IDUs) who share dirty needles or equipment. The National Institute on Drug Abuse (NIDA) offers training opportunities that provide research skills necessary for addressing the joint epidemics of drug abuse and HIV/AIDS. Stronger efforts are needed to train more individuals from affected communities in these specific areas.

NIH ICs need to expand and retain the cadre of new investigators in critically needed research areas, such as behavior sciences. The Behavioral Science Track Award for Rapid Transition (B/START) program, sponsored by NIMH and NIDA, is designed specifically to assist new behavioral scientists in entering the behavioral research environment, through expedited application and review procedures. These programs have to emphasize HIV/AIDS research to allow new investigators to conduct HIV/AIDS studies.

The National Institute of Allergy and Infectious Diseases (NIAID) has developed a new program, Comprehensive International Programs in Research on AIDS (CIPRA), to provide infrastructure and capacity building to institutions from undeveloped countries. Through this mechanism the host country institutions participate in the preparation for large-scale HIV vaccine trials and prevention clinical trials, and also they have the capacity to perform volunteer counseling and testing in their local populations, both to identify new HIV infections and to perform in-country the tests required for vaccine or prevention trials. Other NIH initiatives, similar to CIPRA, need to be developed to focus on the needs in resource-poor countries.

SUPPORT OF ANIMAL FACILITIES

The National Center for Research Resources (NCRR), NIAID, and NCI have several programs in place that are designed to provide NHP for use in pathogenesis studies or in the evaluation of HIV/AIDS vaccine candidates, microbicides, and other physical or chemical barriers. Unfortunately, there has been a shortage of NHP especially of Indian origin; for this reason expanded breeding programs and additional infrastructure are still needed to ensure adequate supplies of these animals. These expansion breeding programs must increase the number of SPF rhesus macaque colonies for AIDS-related research.

NCRR also supports the Chimpanzee Biomedical Research Colonies for AIDS studies through the Regional Primate Research Centers (RPRCs). These RPRCs provide specialized facilities, scientific and technical personnel, breeding programs, and a wide variety of NHP species to support AIDS-related research. NCRR continues to sponsor an initiative to provide non-RPRC investigators with greater access to RPRC resources.

NIAID supports the development of the severe combined immunodeficiency (SCID) mouse model and the research for adaptation of transgenic animal models for HIV infection.

The National Heart, Lung, and Blood Institute (NHLBI) supports animal studies on transfusion-associated HIV infection and AIDS, on the development and evaluation of blood products, and on HIV-specific monoclonal antibody preparations for the prevention or treatment of HIV/AIDS.

INTRAMURAL AND EXTRAMURAL RESEARCH SITE INFRASTRUCTURE

To facilitate the advance of AIDS-related research, NIH has provided funding for the improvement of biomedical research facilities and equipment domestically and on the NIH campus, most recently through the construction of the Vaccine Research Center (VRC) and the

development of a program for Good Laboratory Practices/Good Manufacturing Production (GLP/GMP) of candidate HIV/AIDS vaccines.

NCRR, through the General Clinical Research Centers (GCRCs) across the United States, provides the research infrastructure required for multidisciplinary studies on both children and adults. The IdeA program, also administrated by NCRR, is designed to help enhance the competitiveness for research funding of institutions located in the United States with low success rates for grant applications to NIH. This program should also be implemented to help scientists from minority institutions.

Computers and high-speed computer networks are needed to support HIV protein configuration and structure and also for better and faster communication among scientists at domestic and international sites. The National Library of Medicine (NLM) transition to a system of free Web-based access to MEDLINE and other NLM databases has enabled many investigators to obtain direct access. However, to obtain these benefits, AIDS and other biomedical researchers need to have the essential Internet infrastructure and training so that they can easily access relevant research information and also contribute new information to the ever-expanding AIDS-related databases. This can still be a considerable challenge for researchers in remote, rural, or underserved communities. For researchers in major urban biomedical facilities, Internet access can also be problematic because of peak-hour congestion and the increasing size and complexity of the information being transmitted.

NIH supports numerous repositories that provide resources for HIV/AIDS researchers. NHLBI maintains a repository of blood specimens from individuals with transfusion-associated HIV infection and from AIDS patients who have pulmonary disease. Through the AIDS Research and Reference Reagent Program, NIAID provides specific HIV reagents to investigators worldwide; however, the program needs to be continually expanded to include new reagents. Human specimen banks need to expand to store additional specimens. NHLBI and NIAID have established procedural guidelines to increase access to specimens from their patient cohorts and subjects in clinical trials by qualified investigators not collaborating in the specific studies supported by these Institutes.

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE - A:

Provide training domestically and internationally in biomedical and behavioral research on HIV, with an emphasis on multidisciplinary research in racially and culturally diverse settings domestically, and with attention to the needs of developing countries with high incidence and/or high prevalence of HIV infection.

STRATEGIES:

- Increase predoctoral, doctoral, and postdoctoral training, as well as advanced research training, in the broad range of AIDS-related disciplines.
- Develop and implement programs at domestic institutions, with attention to institutions serving minorities, to provide pre-college training to attract students interested in behavioral and biomedical sciences.
- Expand programs for AIDS-related research to develop culturally appropriate and relevant training models to conduct ongoing research at minority-serving institutions.
- Expand the number of minority supplement awards to enhance the research capacity of minority individuals to make them more competitive for independent funding.
- Fund planning and organizational grants targeting minority institutions and communities. Emphasis should be placed upon grants that develop academy-community partnerships.
- Expand the NIH AIDS LRP to bring scientists and physicians to NIH in order to increase the cadre of trained HIV/AIDS researchers.
- Enhance opportunities and mechanisms for recruiting, training, and retaining biomedical, behavioral, and social scientists in the conduct of interdisciplinary sex and gender analyses in HIV/AIDS research.
- Provide new opportunities and programs to attract newly trained investigators and established researchers from other fields to pursue HIV/AIDS research.

- Develop funding mechanisms to foster better linkages across AIDS-related scientific disciplines, including basic, clinical, epidemiologic, statistical, and behavioral science.
- Ensure adequate resources for the development of equal and productive partnerships between minority and majority institutions and community-based organizations, with the funds located at the minority institution.
- Increase training to strengthen global capacity to conduct multidisciplinary AIDS-related prevention research in developing countries.
- Ensure adequate cultural competency training and ethical training for the conduct of clinical trials in vulnerable populations.
- Provide training in GLP/Good Clinical Practices (GCP) for translational processes and in product development in both domestic and international settings.
- Support the training of biomedical and behavioral scientists in both developed and developing countries in the use of advanced computer and information technologies for HIV-related research.
- Develop and provide integrated training opportunities and information dissemination programs that focus on the ethical issues of clinical trial design and implementation of vaccine and other prevention modalities in at-risk populations, in both domestic and international settings.
- Expand international AIDS training and research programs, coupling the training of scientists from developing countries with increased opportunities to conduct AIDS research when they return to their home countries (e.g., re-entry grants).
- Develop new funding mechanisms and expand existing grant mechanisms, to link U.S. AIDS research scientists, industry partners, and relevant institutions with each other and with investigators and institutions in both developed and developing countries.
- Taking advantage of existing AIDS clinical trials infrastructures, develop specific training programs in clinical trials methodology, including issues related to the design, recruitment, retention, target population dynamics, and analysis of observational studies.

- Expand training programs on the effective use of antiretroviral drugs and prophylactic and therapeutic interventions for co-infections/ opportunistic infections (OIs), as well as adequate monitoring for patient safety.
- Support training opportunities for HIV prevention researchers interested in adding specific methodological skills to their research expertise (e.g., methods to conduct cost-effectiveness analyses, measurement of biologic outcomes in behavioral intervention studies, ethnographic and other qualitative methods, and network analysis).
- Support multidisciplinary training and mentoring programs, with particular emphasis on AIDS-related intervention research such as research on vaccines, microbicides, sexually transmitted diseases (STDs), OIs, interventions to interrupt mother-to-child transmission, behavioral interventions, nutritional interventions, and substance abuse prevention and treatment.
- Facilitate the training of members of affected communities, to make it easier for them to become informed partners in biomedical and behavioral science research.

OBJECTIVE - B:

Establish and maintain the appropriate infrastructure needed to conduct HIV research domestically and internationally with emphasis on populations of high prevalence.

STRATEGIES:

- Invest and expand funding in research infrastructure at minority institutions to increase capacity to support HIV/AIDS research and increase the number of funded minority investigators, for greater involvement and leadership in HIV research.
- Enhance and improve research capacity and infrastructure in resource-poor settings with high HIV incidence, with particular emphasis on construction and operation of facilities for research on HIV prevention, including the development of vaccines and microbicides, as well as clinical trials for therapies and behavioral interventions.
- Develop the infrastructure for the conduct of vaccine trials in domestic and foreign sites, including laboratory capacity, trained scientists and other personnel, appropriate participant cohorts, and mechanisms to address ethical issues such as the implementation of ethical committees and translated human rights documents.
- Enhance and improve research capacity and infrastructure to improve research on AIDS-associated co-infections (hepatitis C virus [HCV], human herpesvirus [HHV-8], tuberculosis [TB], malaria) and malignancies.
- Ensure an adequate infrastructure for producing vaccine candidates for preventive and therapeutic vaccine trials.
- Ensure adequate facilities and resources as well as appropriate ethical and procedural training to conduct HIV-related research in animal models.
- Expand the production of genetically defined SPF NHP, with emphasis on Indian-origin rhesus macaques.
- Develop and characterize appropriate reagents for use in HIV-related research conducted in NHP.

- Support programs that enhance the current research infrastructure, particularly the trans-NIH infrastructure, such as the Centers for AIDS Research (CFARs), the Research Facilities Infrastructure Program (RFIP), and the General Clinical Research Centers (GCRC) Program.

- Increase support for, and awareness of, the Biomedical Technology Resources Program for structural studies of viral and host proteins.

- Provide for the long-term support of advanced in-country research in resource-poor settings participating in priority AIDS-related intervention research, such as methods to interrupt mother-to-child, sexual, or parenteral transmission, or trials of candidate HIV vaccines.

- Increase collaboration between community-based organizations and other Government-supported service providers (such as those funded through the Health Resources and Services Administration, Department of Veterans Affairs, and Centers for Disease Control and Prevention) and academic researchers, to improve the quality and capacity of research endeavors in service settings.

- Establish and support quality-controlled repositories for, and ensure access by, qualified scientists to samples (i.e., serum, peripheral blood mononuclear cell [PBMC], plasma, patient-derived cell lines, cerebrospinal fluid [CSF], semen, breast milk, lymphoid tissues, and other key patient samples) and HIV strains from clinical trials and natural history and epidemiological studies, especially in complex study settings (e.g., mother-to-child transmission studies).

- Maintain the present AIDS-related tumor registries, and ensure linkages between AIDS and cancer registries, for both domestic and international studies.

- Improve and adequately disseminate the process of requesting, prioritizing, and receiving laboratory samples, so that access is as timely and equitable as possible.

- Promote Internet connections and availability of pertinent information technology at health sciences centers, hospitals, outpatient clinics, community-based organizations, and other access points, both domestically and internationally, for HIV-related research and patient care.

- Develop statistical sampling methodologies, data collection protocols, and statistical analysis tools that are easy to use and adaptable to different settings; facilitate efficient statistical analysis and report generation and enhance standardization, when appropriate.
- Promote research in, and application of, medical informatics (e.g., high-performance computing) for HIV/AIDS research and clinical practice in resource-poor settings, both domestically and internationally.
- Enhance coordination and collaboration among other U.S. Government agencies and other international agencies working in the same developing countries.
- Develop efficient and effective systems for collecting and managing multiple-center and single-site clinical and animal model trials data; ensure dissemination of clinical and animal model trial information.

APPENDIX A:

NIH Institutes and Centers

NIH INSTITUTES AND CENTERS

NCI	National Cancer Institute
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NHGRI	National Human Genome Research Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NINDS	National Institute of Neurological Disorders and Stroke
NIDA	National Institute on Drug Abuse
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIMH	National Institute of Mental Health
NINR	National Institute of Nursing Research
NLM	National Library of Medicine
CC	Warren Grant Magnuson Clinical Center
CIT	Center for Information Technology
NCCAM	National Center for Complementary and Alternative Medicine
NCRR	National Center for Research Resources
FIC	Fogarty International Center
CSR	Center for Scientific Review
NCMHD	National Center on Minority Health and Health Disparities
NIBIB	National Institute of Biomedical Imaging and Bioengineering

APPENDIX B:

List of Acronyms

LIST OF ACRONYMS

ART	antiretroviral therapy
ARV	antiretroviral
ACTIS	AIDS Clinical Trials Information Service
AIDS	acquired immunodeficiency syndrome
AITRP	AIDS International Training and Research Program, FIC
ATI	Analytic Treatment Interruption
ATIS	HIV/AIDS Treatment Information Service
BSL	biosafety level
B/START	Behavioral Science Track Award for Rapid Transition
CAB	community advisory board
CAPS	Center for AIDS Prevention Studies (University of California, San Francisco)
CBO	community-based organization
CDC	Centers for Disease Control and Prevention
CFAR	Center for AIDS Research
CIPRA	Comprehensive International Programs for Research on AIDS
CMS	Centers for Medicare and Medicaid Services
CMV	cytomegalovirus
CNS	central nervous system
CSF	cerebrospinal fluid
CTL	cytotoxic T lymphocyte
DC	dendritic cell
ddI	dideoxyinosine
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
EBV	Epstein-Barr virus
FDA	Food and Drug Administration
FIRCA	Fogarty International Research Collaboration Award, FIC
GBV-C	GB virus (hepatitis G)

GCP	Good Clinical Practices
GCRC	General Clinical Research Center
GFATM	Global Fund for AIDS, Tuberculosis, and Malaria
GI	gastrointestinal
GLP/GMP	good laboratory practice/good manufacturing practice
HAART	highly active antiretroviral therapy
HBCU	Historically Black Colleges and Universities
HBV	hepatitis B virus
HCV	hepatitis C virus
HERS	HIV Epidemiology Research Study
HHV	human herpesvirus
HIV	human immunodeficiency virus
HPTN	HIV Prevention Trial Network
HPV	human papillomavirus
HRSA	Health Resources and Services Administration
HVTN	HIV Vaccine Trials Network
IC	Institute and Center
ICC	invasive cervical cancer
IDU	injecting drug user
IRB	institutional review board
IUD	intrauterine device
JCV	JC virus
KS	Kaposi's sarcoma
KSHV	Kaposi's sarcoma herpesvirus
LRP	Loan Repayment Program, NIH
MAC	*Mycobacterium avium* complex
MDR-TB	multidrug-resistant tuberculosis
MHC	major histocompatibility complex
MSM	men who have sex with men
MTCT	mother-to-child transmission

N9	nonoxynol
NAFEO	National Association for Equal Opportunity in Higher Education
NGO	nongovernment organization
NHL	non-Hodgkin's lymphoma
NHP	nonhuman primate
NIH	National Institutes of Health
NMAC	National Minority AIDS Council
NRTIs	nucleoside reverse transcriptase inhibitors
OAR	Office of AIDS Research, NIH
OARAC	Office of AIDS Research Advisory Council
OD	Office of the Director, NIH
OI	opportunistic infection
OPHS	Office of Public Health and Science
PBMC	peripheral blood mononuclear cell
PCP	*pneumocystis carinii* pneumonia
PML	progressive multifocal leukoencephalopathy
RCMI	Research Center in Minority Institution
RCT	randomized clinical trial
RFIP	Research Facilities Infrastructure Program
RNA	ribonucleic acid
RPRC	Regional Primate Research Center
SAMHSA	Substance Abuse and Mental Health Services Administration
SCID	severe combined immunodeficiency
SHIV	chimeric simian/human immunodeficiency virus
SIT	scheduled intermittent therapy
SIV	simian immunodeficiency virus
SPF	specific pathogen-free
STD	sexually transmitted disease
STI	structured treatment interruption; sexually transmitted infection
TB	tuberculosis

Th	T helper cells
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	U.S. Agency for International Development
VEE	Venezuelan equine encephalitis virus
VRC	Vaccine Research Center
WHO	World Health Organization
WIHS	Women's Interagency HIV Study
WITS	Women and Infants Transmission Study
WRAIR	Walter Reed Army Institute for Research